REMARKS

Claims 1-26 are currently pending and under consideration.

Applicants have amended claims 1 and 2 to replace the term "prodrug or derivative" with the term "salt" to overcome the Examiner's rejections.

Applicants have amended claim 21 to correct a typographical error. Therein, applicants have deleted the inadvertent double recitation of the term "method of."

None of these amendments add new matter.

Finally, all of these amendments and claim cancellations are specifically made without prejudice to applicants' ability to seek patents for the cancelled or non-elected subject matter.

The Office Action

35 U.S.C. § 112, first paragraph

Claims 1-26 stand rejected under 35 U.S.C. § 112, first paragraph as lacking enablement. The Examiner contends that although the specification is enabling "for making salts of the claimed compounds," the specification is not enabling for derivatives or prodrugs of the compound (April 11, 2005 Office Action p. 4). Applicants have amended claims 1 and 2 to delete "derivative or prodrug" and substitute therefore "salt," thus obviating these rejections. Support for this amendment may be found in the specifications on p. 23 line 29 to p. 24 line 2.

Claims 13-22 and 24-26 stand rejected under 35 U.S.C. § 112, first paragraph as lacking enablement. The Examiner contends that the specification "while being enabling for treating diabetes," is not enabling for treating "all sorts of diseases for which applicants have not provided any experimental support or nexus" (April 11, 2005 Office Action p. 7). According to the Examiner, the specification provides no "competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host". Id. at 8. The Examiner concludes that, "undue experimentation will be required to practice Applicants' invention" Id. at 8. Applicants traverse.

First, applicants respectfully note that claims 12-14, 19, 20, and 24-26 do not relate to the treatment of any recited diseases. Because these claims do not relate to the treatment of any recited disease, applicants respectfully request that the Examiner withdraw these rejections.

Applicants respectfully submit that the rejected claims are enabled by the specification. As detailed below, inhibition of Auora-2, GSK-3, phosphorylation of tau, and phosphorylation of ß-catenin has been correlated to the treatment of the claimed diseases.

Correlation for the diseases and conditions recited in the rejected claims can be found throughout the specification as originally filed. For example, it has been shown that the phosphorylation of ß-catenin by GSK-3 is associated with increased neuronal cell death. Accordingly, the inhibition of GSK-3 is useful for treating neurological and neurodegenerative disorders. See page 5, lines 1-8. Furthermore, applicants respectfully point out that a well known characteristic of Alzheimer's disease relates to ß-amyloid peptide and the formation of intracellular neurofibrillary tangles caused by the abnormal phosphorylation of Tau protein. See page 4, lines 20-33. As disclosed in the background section of the specification, GSK-3 has been shown to play a key role in this abnormal phosphorylation of Tau protein in both *in vitro* and *in vivo* models. Id. Lovestone reports *in vitro* correlation by showing that both GSK-3a and GSK-3ß induce cellular phosphorylation of tau, and therefore are likely to be the enzymes that induce hyperphosphorylation of tau in Alzheimer's disease. See page 4 lines 20-33. Lovestone et al., *Current Biology* **4**, 1077-86 (1994). Brownlees further reports correlation in *in vivo* models. Brownlees created transgenic mice with human GSK-3ß transgenes and was able to show *in vivo* tau phosphorylation by GSK-3ß in the brain. See page 4 lines 20-33. Brownlees et al., *Neuroreport* **8**, 3251-55 (1997).

The Examiner asserts that no compound has ever been found to treat cancers of all types generally, and therefore, "proof must be provided that this revolutionary assertion has merits." (April 11, 2005 Office Action, p. 8)

Applicants' compounds are applicable to cancer treatments generally. As would be recognized by skilled practitioners, some compounds may not be capable of treating cancer generally because of their mechanism of action. If a compound's mechanism of action is specific for a certain type of cancer, then that compound would not be useful for treating cancer generally. However, if a compound's mechanism of action is general for all cell types, then that compound could be used to treat cancer generally.

Aurora-2 inhibition is an example of a mechanism that is applicable to cancer generally. Aurora-2 kinases are involved in fundamental processes in cell division. Cell division is dependent on the function of Aurora-2 kinase. Aurora-2 activity is therefore essential for cell division. Accordingly, Aurora-2 inhibitors would inhibit cell division in all types of cells.

Therefore, applicants' compounds could be used to treat cancer and, more specifically, the types of cancers recited in claim 16. Accordingly, applicants have enabled the treatment of different types of cancers.

Although the Examiner asserts that the specification is not enabling for the treatment of the diverse disorders of the instant claims, applicants respectfully submit that the models that made up the state of the art at applicants' filing date do indeed correlate inhibition of Aurora-2, GSK-3, phosphorylation of Tau protein, and phosphorylation of ß-catenin with the treatment of the disorders of the instant claims.

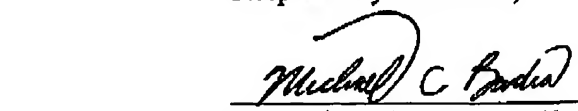
The Examiner contends that factors such as claim breadth, "amount of direction or guidance present," and "the state of the prior art," are sufficiently lacking such that the "unpredictable nature of the art" renders the specification non-enabling for the claimed invention. Id at 9. Applicants would like to point out that the MPEP states that "if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the Examiner has evidence that the model does not correlate." MPEP § 2164.02. Because the models cited in the background section of the present application do correlate the inhibition of protein kinases with the diseases recited by the instant claims, those claims are indeed enabled. Only a reasonable correlation is required - the test does not have to be highly predictive.

Enablement requires an applicant to provide sufficient guidance so that one of skill in the art may use the invention. The MPEP states that "[A]n extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." See MPEP § 2164.06. Applicants do in fact provide sufficient direction and guidance in their specification as originally filed. Specifically, applicants provide the tools to make the compounds of the instant invention (see, e.g., page 64, line 15 to page 68, line 12), to assess the activity of those compounds (see, e.g., page 68, line 15 to page 71, line 4), and to use the compounds (see, e.g., page 17, line 4 to page 27, line 3).

The Examiner has not provided evidence that there is no correlation between the inhibition of Aurora-2, GSK-3, phosphorylation of Tau protein, and phosphorylation of ß-catenin and the methods recited in claims 13-22 and 24-26. Accordingly, applicants respectfully submit that the Examiner has not established a *prima facie* case for non-enablement. For all of the above reasons, applicants respectfully request that the Examiner withdraw these rejections.

Applicants request entry of the above amendments, favorable consideration of the application, and early allowance of the pending claims.

Respectfully submitted,



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